

In the Specification

Amendments to the specification are shown below with insertions indicated by underlining and deletions indicated by strikethrough or double bracketing.

1. Please replace the paragraph beginning on page 14, line 28 with the following paragraph:

Py-rich and TG nucleic acids may also be used for increasing the responsiveness of a cancer cell to a cancer therapy (e.g., an anti-cancer therapy), optionally when the Py-rich or TG immunostimulatory nucleic acid is administered in conjunction with an anti-cancer therapy. The anti-cancer therapy may be a chemotherapy, a vaccine (e.g., an in vitro primed dendritic cell vaccine or a cancer antigen vaccine) or an antibody based therapy. This latter therapy may also involve administering an antibody specific for a cell surface antigen of, for example, a cancer cell, wherein the immune response results in ~~antigen~~ antibody dependent cellular cytotoxicity (ADCC). In one embodiment, the antibody may be selected from the group consisting of ~~Ributaxin~~ Rituxin, Herceptin, Quadramet, Panorex, IDEC-Y2B8, BEC2, C225, Oncolym, SMART M195, ATRAGEN, Ovarex, Bexxar, LDP-03, ior t6, MDX-210, MDX-11, MDX-22, OV103, 3622W94, anti-VEGF, Zenapax, MDX-220, MDX-447, MELIMMUNE-2, MELIMMUNE-1, CEACIDE, Pretarget, NovoMAb-G2, TNT, Gliomab-H, GNI-250, EMD-72000, LymphoCide, CMA 676, Monopharm-C, 4B5, ior egf.r3, ior c5, BABS, anti-FLK-2, MDX-260, ANA Ab, SMART 1D10 Ab, SMART ABL 364 Ab and ImmuRAIT-CEA.

2. Please replace the paragraph beginning on page 24, line 21 with the following paragraph:

The invention in one aspect involves the finding that pyrimidine (Py) rich and preferably thymidine (T) rich nucleic acids as well as nucleic acids that contain TG dinucleotide motifs are effective in mediating immune stimulatory effects. It was known in the prior art that CpG containing nucleic acids are therapeutic and prophylactic compositions that stimulate the immune system to treat cancer, infectious diseases, allergy, asthma and other disorders and to help protect against opportunistic infections following cancer chemotherapies. The strong yet balanced, cellular and humoral immune responses that result from CpG stimulation reflect the body's own natural defense system against invading pathogens and cancerous cells. CpG sequences, while relatively rare in human DNA are commonly found in the DNA of infectious organisms such as bacteria. The human immune system has apparently evolved to recognize

CpG sequences as an early warning sign of infection, and to initiate an immediate and powerful immune response against invading pathogens without causing adverse reactions frequently seen with other immune stimulatory agents. Thus CpG containing nucleic acids, relying on this innate immune defense mechanism, can utilize a unique and natural pathway for immune therapy. The effects of CpG nucleic acids on immune modulation were discovered by the inventor of the instant patent application and have been described extensively in co-pending patent applications, such as U.S. Patent Application Serial Nos: 08/386,063, now US Patent No. 6,194,388, filed on 02/07/95 (and related PCT US95/01570); 08/738,652, now US Patent No. 6,207,646, filed on 10/30/96; 08/960,774, now US Patent No. 6,429,199, filed on 10/30/97 (and related PCT/US97/19791, WO 98/18810); 09/191,170 filed on 11/13/98; 09/030,701, now US Patent No. 6,214,806, filed on 02/25/98 (and related PCT/US98/03678; 09/082,649, now US Patent No. 6,339,068, filed on 05/20/98 (and related PCT/US98/10408); 09/325,193, now US Patent No. 6,405,705, filed on 06/03/99 (and related PCT/US98/04703); 09/286,098, now US Patent No. 6,218,371, filed on 04/02/99 (and related PCT/US99/07335); 09/306,281 filed on 05/06/99 (and related PCT/US99/09863). The entire contents of each of these patents and patent applications is hereby incorporated by reference.

3. Please replace the paragraph beginning on page 36, line 22 with the following paragraph:

Alternatively, nucleic acid stabilization can be accomplished via phosphate backbone modifications. Preferred stabilized nucleic acids of the instant invention have a modified backbone. It has been demonstrated that modification of the nucleic acid backbone provides enhanced activity of the Py-rich and TG nucleic acids when administered *in vivo*. These stabilized structures are preferred because the Py-rich and TG molecules of the invention have at least a partial modified backbone. Py-rich and TG constructs having phosphorothioate linkages provide maximal activity and protect the nucleic acid from degradation by intracellular exo- and endo-nucleases. Other modified nucleic acids include phosphodiester modified nucleic acids, combinations of phosphodiester and phosphorothioate nucleic acid, methylphosphonate, methylphosphorothioate, phosphorodithioate, p-ethoxy, and combinations thereof. Each of these combinations and their particular effects on immune cells is discussed in more detail with respect to CpG nucleic acids in PCT Published Patent Applications PCT/US95/01570 (WO 96/02555) and PCT/US97/19791 (WO 98/18810) claiming priority to U.S. Serial Nos. 08/386,063, now US

Patent No. 6,194,388, and 08/960,774, now US Patent No. 6,239,116, filed on February 7, 1995 and October 30, 1997 respectively, the entire contents of which are hereby incorporated by reference. It is believed that these modified nucleic acids may show more stimulatory activity due to enhanced nuclease resistance, increased cellular uptake, increased protein binding, and/or altered intracellular localization.

4. Please replace the paragraph beginning on page 115, line 5 with the following paragraph:

The stimulation index of a particular immunostimulatory nucleic acid can be tested in various immune cell assays. Preferably, the stimulation index of the immunostimulatory nucleic acid with regard to B cell proliferation is at least about 5, preferably at least about 10, more preferably at least about 15 and most preferably at least about 20 as determined by incorporation of ^3H uridine in a murine B cell culture, which has been contacted with 20 μM of nucleic acid for 20h at 37°C and has been pulsed with 1 μCi of ^3H uridine; and harvested and counted 4h later as described in detail in PCT Published Patent Applications PCT/US95/01570 (WO 96/02555) and PCT/US97/19791 (WO 98/18810) claiming priority to U.S. Serial Nos. 08/386,063, now U.S. Patent No. 6,194,388, and 08/960,774, now U.S. Patent No. 6,239,116, filed on February 7, 1995 and October 30, 1997 respectively. For use *in vivo*, for example, it is important that the immunostimulatory nucleic acids be capable of effectively inducing an immune response, such as, for example, antibody production.